REMARKS/ARGUMENTS

The amendments to the claims are fully supported by the specification and claims as originally filed and do not constitute new matter. Applicants believe that the current amendments place all claims in *prima facie* condition for allowance or, at least, in a better form for consideration on appeal. Accordingly, the consideration and entry of the present amendment after final rejection is respectfully requested.

Applicants expressly reserve the right to pursue any canceled matter in subsequent continuation, divisional, or continuation-in-part applications.

Claims 32, 33, 38, and 44-47 are pending in this application.

Applicants note and appreciate the withdrawal of the earlier objections and rejections under 35 U.S.C. §112, second paragraph and 35 U.S.C. §102(e).

The remaining rejections of Claims 32, 33, 38, and 44-47 under 35 U.S.C. §101, 35 U.S.C. §112, first paragraph, for lack of enablement, and 35 U.S.C. §112, first paragraph, for lack of written description, are addressed below.

I. Information Disclosure Statement

Applicants respectfully thank the Examiner for considering the supplemental information disclosure statement filed on January 26, 2005.

II. Claim Objections

Claim 38 is objected to as being of improper dependent form for failing to further limit the subject matter of a previous claim. The Examiner states that "[c]laim 38 recites the isolated nucleic acid of claim 33 comprising the nucleic acid sequence of SEQ ID NO:375. However, claim 33 also recites an isolated nucleic acid comprising the nucleic acid sequence of SEQ ID NO:375."

Applicants submit that claim 38, as amended herein, recites the isolated nucleic acid of Claim 33 consisting of the nucleic acid sequence of SEQ ID NO:375. Claim 38 further limits the subject matter of Claim 33 and hence is of proper dependent form.

Accordingly, withdrawal of the claim objections is respectfully requested.

III. Claim Rejections Under 35 U.S.C. §101 and §112, First Paragraph (Enablement)

Claims 32, 33, 38, and 44-47 remain rejected under 35 U.S.C. §101 allegedly "because the claimed invention is not supported by a specific, substantial and credible asserted utility or a well-established utility." (Page 3 of the instant Office Action). In particular, regarding the adipocyte glucose/FFA uptake assay (Example 149), the Examiner alleges that "the data do not support the implicit conclusion of the specification that PRO1760 would be useful for the therapeutic treatment of disorders where the inhibition of glucose uptake by adipocytes would be beneficial including, for example, obesity, diabetes, or hyper- or hypo-insulinemia." The Examiner asserts that "[t]he proposed use of the claimed PRO1760 polypeptides and polynucleotides are simply starting points for further research and investigation into potential practical uses of the polypeptides." (Page 5 of the instant Office Action).

Claims 32, 33, 38, and 44-47 also remain rejected under 35 U.S.C. §112, first paragraph, allegedly "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility one skilled in the art clearly would not know how to use the invention." (Page 7 of the instant Office Action).

Applicants respectfully disagree and traverse the rejection. Applicants further submit, for the reasons set forth below, that the specification discloses at least one credible, substantial and specific asserted utility for the claimed polynucleotides.

Applicants respectfully submit that the cancellation of claim 38 renders the rejection of this claim moot.

Utility – Legal Standard

According to 35 U.S.C. § 101:

> Whoever invents or discovers any new and *useful* process, machine, manufacture, or composition of matter, or any new and *useful* improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title. (Emphasis added.)

In interpreting the utility requirement, in *Brenner v. Manson*[1] the Supreme Court held that the quid pro quo contemplated by the U.S. Constitution between the public interest and the interest of the inventors required that a patent applicant disclose a "substantial utility" for his or

[1] *Brenner v. Manson,* 383 U.S. 519, 148 U.S.P.Q. (BNA) 689 (1966).

her invention, i.e. a utility "where specific benefit exists in currently available form."[2] The Court concluded that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. A patent system must be related to the world of commerce rather than the realm of philosophy."[3]

Later, in *Nelson v. Bowler*[4] the CCPA acknowledged that tests evidencing pharmacological activity of a compound may establish practical utility, even though they may not establish a specific therapeutic use. The court held that "since it is crucial to provide researchers with an incentive to disclose pharmaceutical activities in as many compounds as possible, we conclude adequate proof of any such activity constitutes a showing of practical utility."[5] In *Cross v. Iizuka*[6] the CAFC reaffirmed *Nelson*, and added that *in vitro* results might be sufficient to support practical utility, explaining that "*in vitro* testing, in general, is relatively less complex, less time consuming, and less expensive than *in vivo* testing. Moreover, *in vitro* results with the particular pharmacological activity are generally predictive of *in vivo* test results, i.e. there is a reasonable correlation there between."[7] The court perceived "No insurmountable difficulty" in finding that, under appropriate circumstances, "in vitro testing, may establish a practical utility."[8]

The case law has also clearly established that applicants' statements of utility are usually sufficient, unless such statement of utility is unbelievable on its face. [9] The PTO has the initial burden that applicants' claims of usefulness are not believable on their face.[10] In general, an

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[2] *Id.* at 534, 148 U.S.P.Q. (BNA) at 695.

[3] *Id.* at 536, 148 U.S.P.Q. (BNA) at 696.

[4] *Nelson v. Bowler*, 626 F.2d 853, 206 U.S.P.Q. (BNA) 881 (C.C.P.A. 1980).

[5] *Id.* at 856, 206 U.S.P.Q. (BNA) at 883.

[6] *Cross v. Iizuka*, 753 F.2d 1047, 224 U.S.P.Q. (BNA) 739 (Fed. Cir. 1985).

[7] *Id.* at 1050, 224 U.S.P.Q. (BNA) at 747.

[8] *Id.*

[9] *In re Gazave*, 379 F.2d 973, 154 U.S.P.Q. (BNA) 92 (C.C.P.A. 1967).

[10] *Ibid.*

Applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101, "unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope."[11], [12]

Compliance with 35 U.S.C. §101 is a question of fact.[13] The evidentiary standard to be used throughout *ex parte* examination in setting forth a rejection is a preponderance of the totality of the evidence under consideration.[14] Thus, to overcome the presumption of truth that an assertion of utility by the applicant enjoys, the Examiner must establish that it is more likely than not that one of ordinary skill in the art would doubt the truth of the statement of utility. Only after the Examiner made a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift to the applicant. The issue will then be decided on the totality of evidence. The well established case law is clearly reflected in the Utility Examination Guidelines ("Utility Guidelines")[15], which acknowledge that an invention complies with the utility requirement of 35 U.S.C. §101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility." Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that are to be diagnosed.

In explaining the "substantial utility" standard, M.P.E.P. §2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that

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[11] *In re Langer*, 503 F.2d 1380,1391, 183 U.S.P.Q. (BNA) 288, 297 (C.C.P.A. 1974).

[12] *See also In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (C.C.P.A. 1980); *In re Irons*, 340 F.2d 974, 144 USPQ 351 (1965); *In re Sichert*, 566 F.2d 1154, 1159, 196 USPQ 209, 212-13 (C.C.P.A. 1977).

[13] *Raytheon v. Roper*, 724 F.2d 951, 956, 220 U.S.P.Q. (BNA) 592, 596 (Fed. Cir. 1983) cert. denied, 469 US 835 (1984).

[14] *In re Oetiker*, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d (BNA) 1443, 1444 (Fed. Cir. 1992).

[15] 66 Fed. Reg. 1092 (2001).

can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "'substantial'" utility.'"[16] Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement,[17] gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Proper Application of the Legal Standard

The specification provides sufficient disclosure to establish a specific, substantial and credible utility for the claimed polynucleotides for the reasons previously set forth in the Applicants' response filed on January 26, 2005, and below.

The Examiner alleges that "Applicant asserts the PRO1760 polypeptide inhibits glucose uptake in adipocyte cells. If one skilled in the art were to administer the PRO1760 polypeptide of the instant application to a patient with obesity, diabetes, and hyper- or hypo-insulinemia, the PRO1760 polypeptide would exacerbate the condition." The Examiner concludes that "the data do not support the implicit conclusion of the specification that PRO1760 would be useful for the therapeutic treatment of disorders where the inhibition of glucose uptake by adipocytes would be beneficial including, for example, obesity, diabetes or hyper-or hypo-insulinemia." (Page 5 of the instant Office Action).

The Examiner states that "one skilled in the art would want to enhance glucose uptake into adipocyte cells" in order to treat disorders such as diabetes. Applicants respectfully point out that the fact that PRO1760 inhibits glucose uptake does not make it useless in such treatment. One of skill in the art would readily understand that a protein which inhibits glucose uptake into adipocytes is a potential therapeutic target, since blocking the function of this protein would decrease the inhibition, and thus increase glucose uptake into adipocytes. One of skill in the art would further understand that antagonists to the PRO1760 polypeptide include antisense oligonucleotides, such as those which may be derived from the claimed polynucleotides.

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[16] M.P.E.P. §2107.01.

[17] M.P.E.P. §2107 II (B)(1).

Antisense technology and applications are discussed in the specification at, for example, page 310, lines 2-4, page 365 line 2 through page 366 line 4, page 367 lines 24-29, and page 371 line 34 through page 372 line 9. Accordingly, the claimed polynucleotides are useful in the therapeutic treatment of disorders wherein stimulation of glucose uptake by adipocytes is expected to be therapeutically effective, such as obesity, diabetes, and hyper- or hypo-insulinemia.

Applicants also point out that Mueller *et al.* (1998) disclose that inhibitors of adipocyte glucose uptake, including 2-DG, phloretin, and cytocholasin B, inhibit leptin gene expression and leptin secretion from adipocytes. It was known in the art at the time of filing that leptin is involved in the regulation of food intake, energy expenditure, and body fat stores, and that leptin decreases after fasting or caloric restriction and increases a number of hours after refeeding. (Mueller *et al.* (1998), p. 551, col. 1). One of skill in the art would therefore have understood that agents capable of modulating leptin regulation would be useful in investigations regarding the treatment of obesity. Similarly, PRO1760, as an inhibitor of adipocyte glucose uptake, would be useful as a pharmacological tool for investigation of leptin regulation, in the same way as agents already known and used in the art such as 2-DG, phloretin, and cytocholasin B.

The Examiner further asserts that the various references submitted by Applicants allegedly teach different methodologies for the measurement of glucose uptake in adipocyte cells as compared to the glucose assay of the instant specification. The Examiner further asserts that none of the references utilize the stimulatory and inhibitory scale disclosed in the specification. The Examiner asserts that the instant specification "does not report any specific cell numbers or statistical differences and there is no indication in the specification as to statistically how much the PRO1760 inhibited glucose uptake as compared to control."

Applicants respectfully point out that the Examiner has not provided any evidence that the minor variations in assay protocols disclosed by the various references would be expected to alter the assay results. In fact, the main features of the protocol described in the specification are well within the parameters established in the literature. For example, all the cited references utilized adipocytes (Applicants note that the 3T3-F442A cells disclosed in Sandouk *et al.* were differentiated into adipocytes before running the glucose uptake assay). In particular, Mueller *et al.* 1998 use rat adipocytes, as disclosed in the specification. The incubation periods of the

adipocytes prior to measuring glucose uptake range from 15 minutes as disclosed in Sandouk *et al.*, to 24, 48, 72, or 96 hours as disclosed in Mueller *et al* 2000. Thus the 4 and 16 hour incubations used in the specification are well within the range established as valid within the literature. Applicants note that such details as the incubation with metformin or vanadium as disclosed in Mueller *et al.* 2000 are not relevant, as the purpose of the Mueller experiments was specifically to test the effects of metformin or vanadium on glucose transport.

Applicants note that because most of the experiments described in the cited literature were concerned with stimulation of glucose uptake, they do not describe their data in terms of a stimulatory and inhibitory scale. However, the expression of data as a percentage of the control, instead of in specific numbers, is hardly unusual, and a similar scale is used, for example, in Figs. 1-4 of Sandouk *et al.* Further, the specification clearly discloses that the inhibition of glucose transport by PRO1760 was decreased by at least 50% as compared to the control (see the specification at page 512, line 3-6).

Applicants remind the PTO that, as discussed above, the Examiner must establish that it is more likely than not that one of ordinary skill in the art would doubt the truth of the statement of utility. Only after the Examiner made a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift to the applicant. The issue will then be decided on the totality of evidence. Therefore, the legal standard for patentable utility is not absolute certainty. Applicants submit that clear evidence supports the glucose uptake inhibition activity of PRO1760. The Examiner's statements regarding minor assay protocol variations do not suffice to make it more likely than not that one of skill in the art would doubt the truth of this asserted utility of PRO1760 as an inhibitor of glucose uptake.

Accordingly, Applicants respectfully submit that at the effective filing date of the instant application, one of skill in the art would have reasonably accepted that various compounds, such as PRO1760, that are capable of modulating glucose uptake have a substantial, practical, real life utility. The above-mentioned studies have clearly established that the glucose/FFA uptake assay as described in the instant application is a reliable assay system to identify therapeutic agents for treating diseases and conditions such as obesity, diabetes, hyper- or hypo-insulinemia. Therefore, Applicants respectfully submit that a variety of real-life utilities, such as treatments for glucose uptake related diseases, including obesity and diabetes, are envisioned for PRO1760 and the

claimed polynucleotides that encode PRO1760 or a functional variant thereof, based on the glucose/FFA uptake assay results disclosed herein.

In view of the above, Applicants respectfully submit that the specification discloses at least one credible, substantial and specific asserted utility for the PRO1760 polypeptide and for the claimed polynucleotides that encode PRO1760 or a functional variant thereof. Further, based on this utility and the disclosure in the specification, one skilled in the art at the time the application was filed would know how to use the claimed polynucleotides.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present utility rejections under 35 U.S.C. §101 and 35 U.S.C. §112, first paragraph.

IV. Claim Rejections Under 35 U.S.C. §112, First Paragraph (Enablement)

Claims 32 and 44-47 further remain rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement. In particular, the Examiner alleges,

> Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, under experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. (Page 10 of the instant Office Action).

Applicants respectfully disagree and traverse the rejection. For the reasons discussed below, Applicants submit that Claims 32 and 44-47 satisfy the enablement requirement under 35 U.S.C. §112, first paragraph.

The Legal Test for Enablement

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosure provided by applicants coupled with information known in the art at the time the invention was made, without undue experimentation. [18] [19] Accordingly, the test

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[18] M.P.E.P. §2164.01.

[19] *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1998)).

for enablement is not whether any experimentation is necessary, but whether, if experimentation is required, it is undue.[20] The mere fact that an extended period of experimentation is necessary does not make such experimentation undue.[21] [22]

A finding of lack of enablement and a determination that undue experimentation is necessary requires an analysis of a variety of factors *(i.e.,* the *In re* Wands factors). The most important factors that must be considered in this case include 1) the nature of the invention; 2) the level of one of ordinary skill in the art; 3) guidance provided in the specification, 4) the state of the prior art, and 8) the breadth of the claims.

"How a teaching is set forth, by specific example or broad terminology, is not important."[23] [24] "Limitations and examples in the specification do not generally limit what is covered by the claims" M.P.E.P. § 2164.08. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. The legal standard merely requires that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed.[25]

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[20] *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (C.C.P.A. 1976).

[21] *In re Colianni*, 561 F.2d 220, 224, 195 USPQ 150, 153 (C.C.P.A. 1977).

[22] M.P.E.P. §2164.06.

[23] M.P.E..P. §2164.08.

[24] *In re Marzocchi*, 439 F. 2d 220, 223-4, 169 USPQ 367, 370 (C.C.P.A. 1971).

[25] *Enzo Biochem., Inc. v. Calgene, Inc.,* 188 F.3d 1362, 1372 (Fed. Cir. 1999) (quoting *In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991)).

The Disclosure provides sufficient information to enable the claimed invention

First, Applicants respectfully maintain the position that that Claims 32 and 44-47 satisfy the enablement requirement under 35 U.S.C. §112, first paragraph, for the reasons previously set forth in the Applicants' response filed on January 26, 2005.

Second, as discussed above, PRO1760 shows activity as an inhibitor in the adipocyte glucose/FFA uptake assay. Therefore, based on this information one skilled in the art would have known at the time of filing how to use polynucleotides which encode the PRO1760 polypeptide in the therapeutic treatment of disorders wherein stimulation of glucose uptake by adipocytes is expected to be therapeutically effective, such as obesity, diabetes, and hyper- or hypo-insulinemia. For example, the claimed polynucleotides could be used to generate antisense oligonucleotides that block expression of SEQ ID NO:376.

Applicants have provided the native PRO polypeptide sequence SEQ ID NO:376, as well as a DNA sequence, SEQ ID NO:375, which encodes it. The present application also describes methods for identifying proteins which inhibit the uptake of glucose or FFA by adipocyte cells. Example 149 of the present application provides a detailed protocol for the adipocyte glucose/FFA uptake assay. By following the disclosure in the specification, one skilled in the art can easily test whether a polypeptide encoded by a polynucleotide having at least 99% identity to SEQ ID NO:375 inhibits the uptake of glucose or FFA in adipocyte cells. The specification further describes methods for the determination of percent identity between two nucleic acid sequences. (See page 305, line 12 to page 306, line 39). In fact, the specification teaches specific parameters to be associated with the term "percent identity" as applied to the present invention. Accordingly, one of skill in the art could identify whether the variant SEQ ID NO:375 sequence falls within the parameters of the claimed invention. Methods of isolating nucleic acid sequences encoding PRO polypeptides and polypeptide variants are described in the specification at, for example, page 359, lines 9-34; page 364, lines 25-38; and page 481, lines 1-11.

Therefore, Applicants respectfully submit that one of skill in the art could readily test a polypeptide encoded by the variant nucleic acid sequence to determine whether it inhibits the uptake of glucose or FFA by adipocyte cells.by the methods set forth in Example 149. Furthermore, one of ordinary skill in the art has a sufficiently high level of technical competence

to identify nucleic acid sequences with at least 99% identity to SEQ ID NO:375. Accordingly, one of ordinary skill could practice the claimed invention without undue experimentation.

The Examiner asserts that there is a "large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity." (Page 10 of the instant Office Action). Applicants respectfully disagree. Applicants respectfully point out that the number of nucleic acid sequences differing in sequence identity by only 1% from SEQ ID NO:375 is far from infinite. Applicants further note that there are many nucleic acid sequences having at least 99% identity to SEQ ID NO:375 which would not need to be screened for activity, as they encode the identical protein to PRO1760, due to redundancy in the genetic code. One of ordinary skill in the art would know how to make this class of variant polynucleotides without any experimentation at all, based solely upon the provided amino acid sequence of PRO1760 (SEQ ID NO:376) and knowledge of the genetic code. As these variant polynucleotides encode the same protein as does SEQ ID NO:375, they could be used in the same manner. As for those variant polynucleotides that encode proteins differing in sequence from SEQ ID NO:376, it would be a simple matter for one skilled in the art to test the polypeptides to see if they inhibit the uptake of glucose or FFA by adipocyte cells using the methods provided Example 149. This would not require a "large quantity of experimentation."

The Examiner asserts that there is a "lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity" and that the prior art "establishes the unpredictability of the effects of mutation on protein function." (Page 10 of the instant Office Action). Applicants note that a polynucleotide variant having at most 1% difference in sequence from SEQ ID NO:375 must encode a polypeptide having only a limited number of sequence changes from SEQ ID NO:376. In fact, many such polynucleotides will encode proteins that are identical to SEQ ID NO:376, given the known redundancy in the genetic code, and the fact that only a portion of SEQ ID NO:375 comprises the protein coding region. Furthermore, the claims require that the polynucleotide variants encode polypeptides that retain the functional activity of PRO1760, and the specification provides an assay for this activity. One of ordinary skill in the art would easily be able to examine the sequence of a claimed variant polynucleotide to see if it would produce the protein sequence of SEQ ID NO:376. Only those variant polynucleotides encoding sequences not identical to SEQ ID

NO:376 would need to be tested in the provided assay. Thus the specification has provided all the guidance needed to permit one of skill in the art to make and use the claimed variant polynucleotides.

Finally, the Examiner asserts that the claims "fail to recite any structural or functional limitations. In fact, as discussed above, the claims recite both the structural limitation of having at least 99% nucleotide sequence identity with SEQ ID NO:375, and the functional limitation that the encoded polypeptide inhibits the uptake of glucose or FFA by adipocyte cells.

The claims currently recite polynucleotides that encode polypeptide sequences associated with a biological activity. This biological activity together with the well defined relatively high degree of sequence identity and general knowledge in the art at the time the invention was made, is believed to sufficiently define the claimed genus such that, one skilled in the art, at the effective date of the present application, would have known how to make and use the claimed polynucleotide sequences without undue experimentation. As the M.P.E.P. states, "[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation."[26]

As discussed above, a considerable amount of experimentation is permissible, if it is merely routine. Applicants submit that the identification of variant polynucleotides having at least 99% sequence identity to SEQ ID NO:375 wherein the encoded polypeptide inhibits the uptake of glucose or FFA by adipocyte cells can be performed by techniques that were well known in the art at the priority date of this application, and that the performance of such work does not require undue experimentation.

For the above-noted reasons, Applicants respectfully request the Examiner to reconsider and withdraw the enablement rejections under 35 U.S.C. §112, first paragraph.

V. Claim Rejections Under 35 U.S.C. §112, First Paragraph (Written Description)

Claims 32 and 44-47 remain rejected under 35 U.S.C. §112, first paragraph, allegedly as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application

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[26] M.P.E.P. §2164.01 citing *In re Certain Limited-charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff' sub nom. Massachusetts Institute of Technology v A.B. Fortia*, 774 F 2d 1104, 227 USPQ 428 (Fed. Cir. 1985).

was filed, had possession of the claimed invention. In particular, the Examiner alleges that Applicant has not described "a representative number of species that have 99% homology to SEQ ID NO:375, such that it was clear that they were in possession of a genus of polynucleotides functionally similar to SEQ ID NO:375." (Page 11 of the instant Office Action).

Applicants respectfully disagree and traverse the rejection. For the reasons discussed below, Applicants respectfully submit that Claims 32 and 44-47 satisfy the written description requirement under 35 U.S.C. §112, first paragraph

The Legal Test for Written Description

The well-established test for sufficiency of support under the written description requirement of 35 U.S.C. §112, first paragraph is "whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language."[27] [28] The adequacy of written description support is a factual issue and is to be determined on a case-by-case basis.[29] The factual determination in a written description analysis depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. [30] [31]

In *Environmental Designs, Ltd. v. Union Oil Co.*,[32] , the Federal Circuit held, "Factors that may be considered in determining level of ordinary skill in the art include (1) the educational level of the inventor; (2) type of problems encountered in the art; (3) prior art solutions to those problems; (4) rapidity with which innovations are made; (5) sophistication of the technology; and

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[27] *In re Kaslow*, 707 F.2d 1366, 1374, 212 USPQ 1089, 1096 (Fed. Cir. 1983).

[28] *See also Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116 (Fed. Cir. 1991).

[29] *See e.g., Vas-Cath*, 935 F.2d at 1563; 19 USPQ2d at 1116.

[30] *Union Oil v. Atlantic Richfield Co.*, 208 F.2d 989, 996 (Fed. Cir. 2000).

[31] *See also* M.P.E..P. §2163 II(A).

[32] 713 F.2d 693, 696, 218 USPQ 865, 868 (Fed. Cir. 1983), *cert. denied*, 464 U.S. 1043 (1984).

(6) educational level of active workers in the field." (Emphasis added).[33] Further, The "hypothetical 'person having ordinary skill in the art' to which the claimed subject matter pertains would, of necessity have the capability of understanding the scientific and engineering principles applicable to the pertinent art."[34] [35]

The specification provides sufficient written description for the claimed invention

First, Applicants respectfully maintain the position that that Claims 32 and 44-47 satisfy the written description requirement under 35 U.S.C. §112, first paragraph, for the reasons previously set forth in the Applicants' response filed on January 26, 2005.

Second, Applicants respectfully submit that the instant specification evidences the actual reduction to practice of a full-length PRO1760 polypeptide of SEQ ID NO:376, as well as the full length polynucleotide of SEQ ID NO:375 which encodes PRO1760. Thus, the genus of polynucleotides with at least 99% sequence identity to SEQ ID NO:375 wherein the encoded polypeptide inhibits the uptake of glucose or FFA by adipocyte cells would meet the requirement of 35 U.S.C. §112, first paragraph, as providing adequate written description.

As mentioned above, Applicants respectfully point out that the instant specification describes methods for the determination of percent identity between two nucleic acid sequences (please see the discussion under Enablement). The specification describes methods for one of ordinary skill in the art to identify polynucleotide sequences having at least 99% identity to SEQ ID NO:375 wherein the encoded protein inhibits the uptake of glucose or FFA by adipocyte cells. Specifically, Example 149 sets forth an assay for determining whether a polypeptide encoded by a polynucleotide having at least 99% sequence identity to SEQ ID NO:375 inhibits the uptake of glucose or FFA by adipocyte cells. Thus one of ordinary skill in the art would have understood at the time of filing what was encompassed by the claims.

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[33] *See also* M.P.E.P. §2141.03.

[34] *Ex parte Hiyamizu*, 10 USPQ2d 1393, 1394 (Bd. Pat. App. & Inter. 1988) (emphasis added).

[35] *See also* M.P.E.P. §2141.03.

The Examiner asserts that "one skilled in the art could not envision the detailed chemical structure of all or a significant number of encompassed PRO1760 polynucleotides, and therefore, would not know how to make or use them." (Page 11 of the instant Office Action). Applicants respectfully point out that one of ordinary skill in the art could easily envision the detailed structure of polynucleotides having at least 99% sequence identity to SEQ ID NO:375 wherein the encoded protein inhibits the uptake of glucose or FFA by adipocyte cells. For example, it would be clear to one of skill in the art that polynucleotides having at least 99% sequence identity to SEQ ID NO:375 and encoding the same PRO1760 polypeptide would be encompassed by the claims. The skilled artisan would recognize these polynucleotides by examining the sequence of PRO1760 (provided in the specification as SEQ ID NO:376) and using knowledge of the genetic code to determine alterations to SEQ ID NO:375 that would not affect the encoded polypeptide sequence. The skilled artisan could easily write out a listing of all such polynucleotides. Because these polynucleotides can so readily be envisioned, there is no need to actually list all such sequences, and to do so would needlessly clutter the specification.

Further, Applicants respectfully direct the Examiner's attention to Example 14 of the Written Description Guidelines issued by the U.S. Patent Office Example 14 of the Written Description Guidelines clearly states that protein variants meet the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention, even if the specification contemplates but does not exemplify variants of the protein if (1) the procedures for making such variant proteins is routine in the art, (2) the specification provides an assay for detecting the functional activity of the protein, and (3) the variant proteins possess the functional activity and at least 95% sequence identity to the reference sequence. Applicants submit that the instant application evidences the reduction to practice of a full-length PRO1760 polypeptide of SEQ ID NO:376, with or without its signal sequence, and its encoding nucleic acid sequence of SEQ ID NO:375. In addition, the specification provides detailed description about the cloning of nucleic acid variants and describes the adipocyte glucose/FFA uptake assay for testing the activity of the encoded polypeptides. Thus, Applicants submit that the genus of nucleic acids that code for the polypeptide of SEQ ID NO:376, or nucleic acid variants having at least 99% sequence identity to SEQ ID NO:375, wherein the encoded polypeptides possess the functional

activity of inhibiting glucose or free fatty acid uptake in adipocytes, would meet the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description.

Accordingly, the specification provides adequate written description for polynucleotides having at least 99% identity to SEQ ID NO:375 wherein the encoded polypeptide inhibits the uptake of glucose or FFA by adipocyte cells. For the above reasons, Applicants respectfully request the Examiner to reconsider and withdraw the written description rejections under 35 U.S.C. §112, first paragraph.

CONCLUSION

All claims pending in the present application are believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (referencing Attorney's Docket No. **39780-2830 P1C66**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: June 3, 2005

By: _____
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